

301 Assessment of surfactants for Salbutanol sulphate formulation

Formulation

Salbutanol Sulphate (g)	0.012
Surfactant (g)	0.005
Ethanol (g)	0.58
P134a (g)	5.22

The above formulation was prepared with various surfactants using the method as follows:-

Surfactant weighed in beaker, then salbutanol sulphate, slight less than the required amount of ethanol was added. Ultrason applied for approx 20 secs then silversen mixing for approx 30 secs. The concentrate was added to a bottle and the amount of ethanol made up to ^{the} correct weight.

A non metering valve was fitted and P134a was pressure filled to the correct weight.

PET bottles were used initially but on standing there was a loss of propellant, therefore glass bottles were used and the formulation was doubled.

Surfactant	Description of Suspension
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Span 85 Soluble in ethanol. Good suspension (best of Spans) slowly sediments. Clear supernatant after standing overnight. Coarse floccules sediment after 30 secs.

Fairly small volume of sediment

Span 80 Soluble in ethanol. Good suspension but not as good as Span 85, slowly sediments. Clear supernatant after standing overnight. Coarse floccules sediment after 30 secs. Small

volume of sediment.

<u>LAB. BOOK ENTRY</u>

Signed by: P.A. McGahan
Witnessed by: P.D. Hodson
Date: 22.2.89

Surfactant

Description of Suspension

Span 20

Soluble in ethanol. Good suspension, slowly sediments. Clear supernatant after standing overnight. Coarse flocs sediment after 30secs. Very small volume sediment, smaller than other Spans and Tweens.

Tween 20

Tween 20 slightly better formulation than Tween 80. Both soluble in ethanol. Good suspension slowly sediments to give a loose sediment with small volume. Clear supernatant on standing overnight. Coarse flocs sediment after 30secs.

Oleic acid:

Soluble in ethanol. Good suspension, as good as Span 85, better than other Spans and Tweens. Fairly small volume of sediment, clear supernatant on standing overnight. Large flocs sediment after 30 secs.

Brij 92

Brij 72

Soluble in ethanol. Good suspension, fine initially gradually flocculates, large flocs settle after 20 secs. Clear supernatant on standing overnight. Brij 92 gives a slightly more stable formulation. Small volume of sediment.

Genopol - o - 020

Soluble in ethanol. Good suspension fine particles gradually sediment ~ 20 secs. Clear supernatant on standing overnight. Not as stable a formulation as Brij 92.

Diethylenglycol
Dioleate

Soluble in ethanol. Fair suspension, fine particles flocculate and sediment out after approx 30secs. Clear supernatant on standing overnight. Small volume

SUSPENSION BOOK ENTRY

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Date: 22.2.71

Surfactant	Description of Suspension
Tetrahydrofurfuryl Oleate	Soluble in ethanol. Good suspension. Floccules slowly sediment after approx. 30secs. Clear supernatant on standing overnight. Small volume sediment.
Ethyl Oleate	Soluble in ethanol. Good suspension, coarse floccules, settle after 20secs. Clear supernatant on standing overnight.
Glyceryl Mono Oleate	Soluble in ethanol. Good suspension, finer floccules, settle after 20secs. Clear supernatant on standing overnight.
Glyceryl Mono Laurate	Soluble in ethanol. Good suspension, coarse flocs settle after 20secs. Clear supernatant on standing overnight. Small volume sediments.
Glyceryl Mono Stearate	Not Soluble in ethanol. Large floccules settle after 20secs. Clear supernatant on standing overnight. Large volume sediment compacts slowly. Glyceryl mono stearate forms suspension with silverstein mixing.
Glyceryl Monoricinoleate	Soluble in ethanol. Flocs form quickly larger flocs sediment after 30secs. Clear supernatant on standing overnight.
Cetyl Alcohol	Soluble in ethanol. Flocs form quickly larger flocs sediment after 40secs.
<u>TIME 300g S.AU</u>	Slightly cloudy supernatant on standing. Small volume sediment.

<u>LAB. BOOK ENTRY</u>	
Signed by: P.A. McGahan	
Witnessed by: P.D. Hodson	
Date:	22.2.89

Surfactant

Description of Suspension.

Cetyl Pyridinium Chloride

This surfactant was micronised. Soluble in ethanol. Fine suspension, most sediments after 40 secs. Very small volume sediment. but not as small as synperonics.

Synperonics L61

L64

L92

P94

All soluble and gave suspensions with similar characteristics. Quickly flocculate (after 10 secs) Large flocs sediment after 30 secs cloudy supernatant initially, clears on standing overnight.

Very Small volume sediments.

FC 807 organic extract.

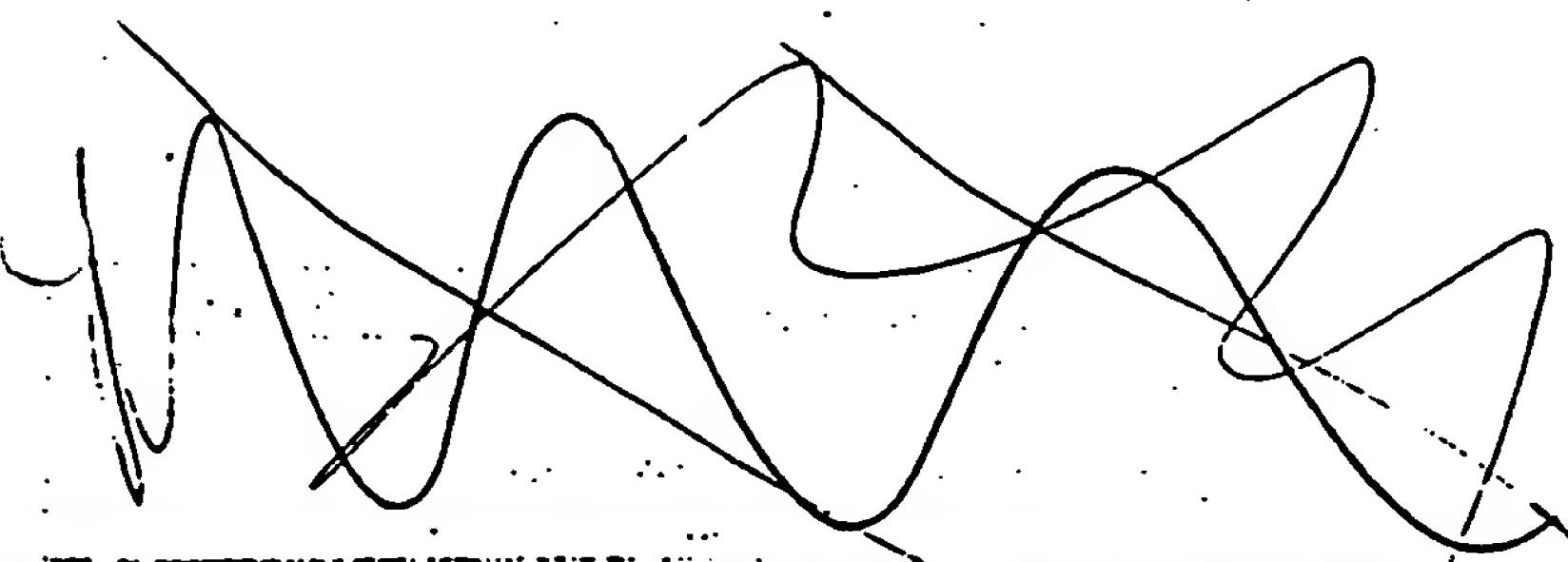
Soluble in ethanol Good suspension flocs sediment after 30 secs. Clear supernatant on standing overnight. Small volume sediment.

Placebo (no surfactant)

Good suspension slowly sediments cloudy supernatant initially clears on standing. Small volume of sediment.

All surfactants used produced similarly stable suspensions, some were slightly better than others but none were outstanding.

The formulation with no surfactant was as good as the better surfactants if not better in that it had a slightly slower sedimentation rate.



LAB. BOOK ENTR:

Signed by: P A McGahan
Witnessed by: P D Hudson.
Date: 22.2.89.

Exhibit 1

In addition formulations were prepared using other surfactants to the formula as follows i.e. with a higher level of surfactant

Salbutamol Sulphate (g)	0.012
Surfactant (g)	0.012
Ethanol (g)	0.58
P134ta (g)	5.22

Glyceryl Trideate (Olive Oil)	Quickly forms medium sized floccles which begin to sediment after 20 secs. Easily resuspended. Small volume sediment
Isopropyl Myristate	Fine suspension begins to sediment after 25 secs. Small volume sediment easily resuspends.
EG 400	Fine suspension begins to sediment after 20 secs. Small volume sediment easily resuspends.
Brij 30	Fine suspension begins to sediment after 25 secs. Small volume sediment, easily resuspends.
Stearyl Alcohol	Stearyl alcohol is soluble in ethanol. Medium size flocs begin to sediment after 20 secs. Small volume sediment, easily resuspends.
Stearic Acid	Large flocs form and begin to sediment after 25 secs. Small volume sediment easily resuspends.

LAB. BOOK ENTRY

Signed by: P A McGahan
Witnessed by: P D Heaton
Date: 20.3.89

Span 85	Large flocs form and sediment rapidly. Large volume sediment in comparison to other formulations. Easily resuspends.
Oleic Acid	Fine suspension begins to sediment after 20secs Small volume sediment easily resuspends.
FC 807	Fine suspension begins to sediment after 20sec Small volume sediment easily resuspends.
Lecithin Eptikwon	Little difference between Lecithin and Synthetic Lecithin. Medium sized flocs form which begin to sediment after 15secs. Small volume sediment easily resuspends.
Synthetic Lecithin (Palmitoyl Oleoyl Glycerophosphatidylcholine)	Medium sized flocs form which begin to sediment after 15secs. Small volume sediment easily resuspends.

After preparation in glass bottles the formulations were transferred to cans by chill down method. Valves were function tested with several doses fired and all found to be satisfactory. 4" slides were prepared and examined under the microscope. Most formulations had the majority of particles less than 10μ with a few crystals approx 10μ. No agglomerates. However in the formulations with lecithin 1 or 2 agglomerates were observed.

In the formulation with Span 85 many agglomerates seen with few crystals, a very poor formulation.

These samples were placed on storage at 40° 87% to be ~~re-examined~~ in two weeks time.

Mr. George
A. T. Johnson,
1989

LAB. BOOK ENTRY

Signed by: PA McGahan
Witnessed by: PJ Hodson
Date: 20.3.89